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OBITUARY

Sueharu Horinouchi (1 January 1952–12 July 2009)

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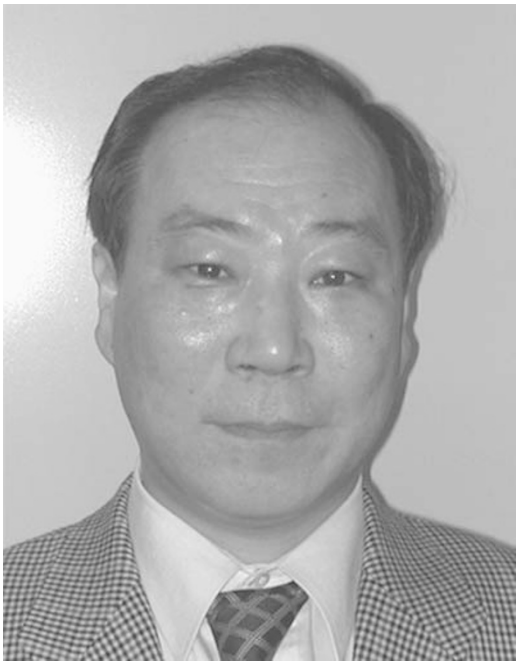
Professor Sueharu Horinouchi passed away on 12 July 2009 at the age of 57 after a 2-year struggle with a severe illness.

Professor Horinouchi was born on 1 January 1952 in Kagoshima Prefecture in the south part of Kyushu Island, Japan. He lived in Kagoshima for 18 years and moved to Tokyo to enter the University of Tokyo in 1970. In 1973, he became a member of the *Hakko* (a Japanese word that means fermentation and applied microbiology) Laboratory as an undergraduate student and was supervised by Professor Kei Arima. He studied microbiology and molecular biology in the same laboratory and received a PhD from the University of Tokyo in 1979. This was the age when recombinant DNA technology was launched, and the *Hakko* Laboratory struggled to establish experimental systems for this new technology. Dr Horinouchi contributed to many technological breakthroughs and made an original observation indicating that *Streptomyces* drug-resistant genes are not expressed in *Escherichia coli*. This was the earliest observation regarding species barriers for gene expression.

From 1979 to 1981, he worked as a postdoctoral research fellow in Professor Bernard Weisblum's laboratory at the University of Wisconsin, Madison, WI, USA. During these 2 years, he made his first major discovery: that of revealing a novel translational regulation mechanism for the expression of an erythromycin resistance gene. This work is described in Dr Watson's popular textbook, *Molecular Biology of the Gene*.

In 1981, Dr Horinouchi returned to the University of Tokyo as an assistant professor in the *Hakko* Laboratory, where Teruhiko Beppu was appointed as a full professor in 1977, succeeding Professor Arima. Dr Horinouchi worked with Professor Beppu for 13 years, and took responsibility for research on the genetics of *Streptomyces* in the laboratory. After he became an associate professor in 1987, he contributed to many other studies in the laboratory. Finally, he was appointed a full professor in the *Hakko* Laboratory in 1994, succeeding Professor Beppu, and served for 15 years as a full professor before his death.

One of his great achievements was to reveal the A-factor regulatory cascade in a streptomycin producer, *Streptomyces griseus*. A-factor was initially discovered by Dr Khokhlov in Moscow in the late 1960s as a microbial hormone that triggers both morphological development and secondary metabolism in *S. griseus*. Professor Beppu rediscovered A-factor in the early 1980s and began studying it with then-assistant professor, Dr Horinouchi. The A-factor regulatory cascade emerged in a long string of important papers in leading journals authored by Dr Horinouchi's group. When the A-factor, which is produced in a growth-dependent manner, reaches a critical concentration, as low as



10^{-9} M in *S. griseus*, it binds to the A-factor-specific receptor (ArpA), which binds to the *adpA* promoter and dissociates ArpA from the promoter. The transcriptional activator AdpA then activates the transcription of a number of genes required for secondary metabolism and morphological differentiation, forming an AdpA regulon, which includes *strR* encoding the pathway-specific transcriptional activator for streptomycin biosynthesis. This explains the long-standing question, 'How does A-factor induce streptomycin production at the molecular level?' Dr Horinouchi had a key role in the *S. griseus* genome sequence project. The complete genome sequence permitted a comprehensive analysis of the A-factor regulatory cascade, and the overall picture of the cascade was revealed. Another important achievement by Dr Horinouchi was the discovery of a eukaryotic Ser/Thr protein kinase (AfsK) in *Streptomyces coelicolor* A3(2). AfsK is activated by self-phosphorylation at Thr-168, and it phosphorylates a pleiotropic regulator, AfsR, which is involved in secondary metabolism in *S. coelicolor* A3(2). Although Dr Horinouchi really loved *Streptomyces*, his research was not restricted to this genus. He studied acetic acid fermentation by acetic acid bacteria and the genetics of a

zygomycetous fungus, *Rizomucor*. After he became a full professor, he also studied the molecular biology of eukaryotic cells using chemical genetics with then-associate professor, Minoru Yoshida.

Dr Horinouchi worked not only on basic science but also on applied science. One of his application-oriented studies involved the production of plant-specific polyketides by fermentation. Using new metabolic engineering techniques, he successfully produced 136 plant-specific polyketides (flavonoids, stilbenoids and curcuminoids), including many unnatural ones. Last year, he wrote a review of this work in *The Journal of Antibiotics*, titled 'Combinatorial biosynthesis of non-bacterial and unnatural flavonoids, stilbenoids, and curcuminoids by microorganisms' (Vol 61(12), pp 709–728). He believed that useful medicinal compounds could be discovered from the developing library of polyketides produced by fermentation.

Professor Horinouchi was one of the leaders of microbiology in Japan. He held important posts in various societies. He was a member of the Editorial Board of *The Journal of Antibiotics* from 1995 to 2009. He won several important awards, including The Sumiki–Umezawa Memorial Award (1991) from the Japan Antibiotics Research Association; The Society for Actinomycetes Japan Award (1994); The Kei Arima Memorial Japan Bioindustry Association Award (2004); and The Japan Bioscience, Biotechnology and Agrochemistry Society Award (2006). Although his untimely passing will be a great loss for several societies in the microbiology field not only in Japan but also in the world, his spirit will be succeeded by his many followers.

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